PROCEEDINGS

OF

The American Microscopical Society

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THE ANNUAL ADDRESS OF THE PRESIDING OFFICER.*

THE NATURAL IN DISEASE.

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It is specified in the constitution of this society, that the president shall deliver an address at its annual meeting. In the past, these have consisted of a presentation of the results of personal investigation, a resume of the present knowledge of the particular subject in which the speaker happened to be most interested, or, a more philosophic dissertation on some phase of micro-biology. The most arduous of the duties of the president seems to have become the preparation of such a treatise, and its reception the special enjoyment of these annual gatherings. This year, however, there has happened a sad incident which has marred the pleasure of this meeting, and which has snatched from us the president's annual offering.

In the death of President Kellicott, this society has lost one of its early members and a loyal friend, and the world a most

*The sudden death of President Kellicott in April last, and the impaired health of the first vice president, caused, for the first time in the history of the society, the duties of the presiding officer to fall upon the second vice president.

enthusiastic student of natural history. He was a man whose life was spent in nature's great laboratory, and if he had been spared to address us on this occasion, we would have listened to an important chapter from nature study. He taught during his lifetime the existence of higher and nobler ideals. Personally, I am much indebted to the living influence of his forceful character and, if perchance, in my feebleness in trying to do as he would have wished, I shall be so fortunate as to kindle anew or deepen your interest in pure or applied biology, cherish the thought as a reflected message from him who would, had God willed, instructed us this hour.

Under the trying circumstances, I had some difficulty in selecting a topic for this formal address. The little time since this unexpected duty fell to me has been so overcrowded with other and more imperative duties, that it was impossible to carry out a new, or even complete, any line of investigation, the results of which could be used on this occasion. Likewise it was too brief for preparing a discussion on any of the broader and more fundamental problems centered in any of the sciences represented in our society. It so happened, however, that following this call to duty, I had occasion to adjust a course of instruction in comparative bacteriology, to meet the needs of students of human medicine, and, at the same time, to fill it full for those who were seeking knowledge in comparative pathology. In working out this actual and seemingly difficult problem, the subject as announced suggested itself and in its somewhat popular consideration I ask your indulgence.

If, in my selection, I seem to have failed in appreciating the fitness of things, and to have brought before a society which deals in pure science, a jungle of practical "isms", I must ask, impertinent as it may seem, what is the aim, the ultimate purpose, of the observations and rich discoveries in physiology, in in anatomy, in botany, and to a less extent in pathology as carefully recorded in our annual volumes? Why have so many workers in biology striven with untiring energy to discover the hidden structure or to learn the vital purpose of the cells of the living body, not only in man but in the lowlier animals and in

plants as well. The technical and enthusiastic biologist sometimes hesitates when he is asked to point out the practical significance of his investigations; but, the sober answer of the devotee of each of the varied branches of human research assures us that it is for bettering human existence. How this is to be brought about, is in the beginning unthought of, but we all share in the consciousness that the discovery of a new fact, the crystalizing of a new truth, the extending of our horizon into nature's processes by a single ray, adds something to the sum total of human enjoyment.

Undoubtedly, the primary purpose of this organization was to hasten the perfection and application of the microscope. This instrument which has passed through a most perfect evolution, rising from a simple lens beset with errors in contour, to a complicated instrument, not only for magnification but of precision as well. By its aid, the ultimate cells in the structure of the organic world are being measured and delineated with mathematical exactness. However, time has shown, that equally as important a result issuing from this band of workers has been a share in the elucidation of many obscure problems in the realm of natural history. Although in themselves they are seemingly remote from the ideals of the utilitarian, they have little by little illuminated the conditions connecting the normal with the abnormal until many of the cords which bound pain and suffering to mankind have snapped asunder.

There is, perhaps, nothing in the evolution of human thought which stands out more conspicuously than the idea of the supernatural in producing and curing disease. In Egypt, in India, in Persia and in China, the healing art was entrusted to the priestly class. In the middle centuries the faith in the supernatural cause of disease and belief in fetish cures became so strong, that there was something irreligious in seeking cure by natural means. At one time it is affirmed that physicians were forbidden to treat the sick without calling in ecclesiastical advice. As a rule, the leaders in theology discouraged the belief that diseases were caused by natural agencies. It is largely due to this, that it was possible for the vast system of "pas-

toral medicine'' so powerful in the middle ages, and in certain phases continuing even at the present time to exist. Monasteries possessed healing relics which turned vast treasures into their coffers. The skulls of the three wise men of the East so carefull encased in the cathedral of Cologne, and the bones from plundered cemeteries hung on the walls of the churches of St. Gereon and of St. Ursula are said to have been potent agencies in healing the sick and remunerating the priests. Even Martin Luther, the great champion of religious liberty, ascribed his own diseases to "Devil's spells", and declared that "Satan produces all the maladies which afflict mankind".

In opposition to the idea of the supernatural as the immediate and specific cause of disease, there sprang up with the teachings of Hippocrates, a different and more rational theory. Living as he did in that early age of lofty thought and philosophy, he broke away from the traditional theories and laid the foundations of medical science upon experience, observation and reason. The school of Alexandria promulgated this theory. Thus five hundred years before the Christian Era, the minds of a few men were turned toward the natural in disease; but the little which had been gained seemed to have been lost in the middle ages with the development of the new interpretation of disease as a product of satanic forces, and the restoration to health the special act of a Divine agency.

For nearly two thousand years after Hippocrates, the condition of the science and of the art of medicine was primitive indeed. Like those poor people of to-day who try to charm away disease with a "madstone", the sick and injured were the victims of circumstances, or, rather, they lived or died as the chance may have been. We sometimes forget that many people in the present generation entertain vagaries concerning the cause of physical disorders which are quite as astonishing as those cherished more generally centuries ago. The time seems to be ripe when biology should claim the abnormal and its causes as a complement to the normal. Do we not find in the abnormal as elsewhere, that "Nature is neither kind nor cruel, but simply obedient to law, and, therefore, consistent"! The

burden of the thought which led to the selection of my subject, was the vast indebtedness of the world to biology for interpreting the nature and finding the cause of so many of the diseases which afflict the vegetable and animal kingdoms. To this should be added the desire of every honest physician and every thoughtful teacher of biology to have all who will feel that disease is a natural product, that its coming and its going depend largely upon conditions which are possible for man to find out and control. I do not wish to be understood by this that it is within man's power to prolong life indefinitely, but rather, that those maladies which shorten our allotted three score years and ten upon earth, are, for the greater part, preventable.

The early history of medicine is confined in the biography of a few men. Schools were founded on men, not on principles until the increeping of error and false hypotheses became more potent than truth itself. But worse than this, and more to be regretted than all the other undesirable influences of those early teachings, there grew up in the public mind that greatest of misconceptions, the belief in disease as an entity, "an evil spirit to be exorcised and driven out by drugs". The superficial observer recognizes only results, he is content with knowing the end, never seeking the causes. Results are his ultimatum, for factors and forces have not disturbed the quietude of his mental processes.

As we approach the early dawn of modern medicine, we find Sydenham going to nature for an explanation of the morbid processes which confront the practitioner. He laid down and acted upon the fundamental proposition that, "All diseases should be described as objects of natural history". In discussing the method for the study of medicine, he states, "In writing, therefore, such a natural history of diseases, every merely philosophical hypothesis should be set aside, and the manifest and natural phenomena, however minute, should be noted with the utmost exactness". His theories were rigorously opposed by Morton and others who considered all diseases to be "poisoning of the vital spirits", but he became the standard bearer of his time in returning to the methods of Hippocrates whose

method and art of healing "were founded on the nature of things, and on the limits of human ability".

Among those who were foremost in subduing prejudices and eliminating false hypotheses which smothered the study of disease for so many centuries, should be mentioned John Hunter. He may be known to some of us better as naturalist than physician. It is, perhaps, through his great achievements as student of nature, that he exercised his greatest power. He was a pathologist, but he looked upon morbid processes as a part of the great whole, governed by law, but which could not be understood until the facts were secured, tabulated and systematized. His untiring industry and peculiarily interesting experiments, attracted men to him, and it has been well said that, "he made all physicians naturalists". Certain it was, that in his generation and that immediately following him, many of the successful practitioners became distinguished as students of nature.

If we should trace from the beginning the progress in human pathology, we would find that the great landmarks are the discoveries and the works of biologically trained men who were devotees of pure science, and not the results of those who made technical utility their guiding principle. What would modern medicine and surgery be if we should strip from them all of these useful and beneficient applications which have come from the discoveries of Galvani, Volta, Harvey, Priestly, Magendie, Claude Bernard and many others, to say nothing of the wonderful revelations which have been made in more recent years? The revolution in surgery wrought by Lister has its origin in the discoveries made by Pasteur, a chemist and biologist. It is an interesting fact, that those medical schools which have advanced the science of medicine most, have been associated with great Universities which offered special inducements for biologic study. While there has existed on the one hand a feeling that the science of medicine is something more enobling than a part of pure biology, and on the other, the technical botanist and zoologist sometimes frown upon the seeming looseness of the science of the healing art, there is much in old asso-

ciations to increase a mutual sympathy. Before there was a school of botany or zoology, or of law, or even of theology, there was a school of medicine. For centuries, all there was of biology was clustered around the teachers of medicine, many of whom advanced our knowledge of disease with most astonishing rapidity by means of their discoveries as biologists. Pathology itself which is the pure science of medicine as contrasted with the healing art, was without a name even, until a better knowledge of the normal revealed the existence here and there of the abnormal. These deformities were relegated to a department by themselves where they remained undisturbed until finally they attracted the attention of a few zealous students of nature, who, in the course of time, have shown that the abnormal holds an equal position with the normal in the great group of Natural Sciences.

It would be interesting to continue this retrospect and learn how perfectly the premises, that "disease is a part of natural history", as it is now understood, was heralded by those fathers of modern medicine who saw deeper into the nature of the abnormal than the average man. However, the brilliancy of those early prophecies, those beacon lights of the new pathology, no matter how bright they might have been, are as shadows compared with the actual that has happened in the evolution of pathology. It is exceedingly modest to affirm that the investigations and experiments which have been made during the last fifty years have done more than all the observations of the preceding centuries to raise pathology from the realm of superstition and darkness, to conditions of light and exactness. Illustrations are numerous, but perhaps the specific diseases offer the most striking ones. From the very dawn of medical history to the brilliant investigations of Davaine, published in 1863, anthrax had decimated again and again the flocks and shepherds of the civilized world. Its nature was unknown, its cause was shrouded in mystery, and its coming was supposed to be an expression of rebuke from angry gods or enraged devils. Since 1863 the specific cause of ths disease has been discovered, and its terrors have been allayed by prohibiting its appearance.

Tuberculosis, Asiatic cholera, and the pest of India, afford similar illustrations of human vagueness in the past concerning the nature of disease and the feeble faith in man's ability to prevent or control them. We are no longer paralyzed by fear of epidemics of these terrible diseases foı their causes have been captured and brought largely within the control of man, and today these specific agents are growing, somewhat as curiosities, in peaceful colonies in scores of our biologic laboratories. Where in the history of man's advancement can greater victories be found?

Definite knowledge which led to the demonstration of morbid processes, as products of natural agencies, began to accumulate with increased rapidity, near the dawn of the present century. In fact, this new theory took a definite position just as soon as biologists, physicists, and the makers of instruments of precision made it possible for the pathologist to study intelligently the finer structure of the abnormal. The progress of pathology has been paralleled with the progress of philosophy itself, "system succeeding system in genetic order." It was impossible, therefore, from the very nature of things, to have established a theory respecting the etiology of disease based upon natural or specific causes, so long as the reasoning and the philosophy of the day did not admit such a cause to be necessary. What could a rational interpreter of diseases do when the scientists advocated and the populace believed, not only in the possibility of, but in the actual every day happening of spontaneous generation? With the fall of that theory, micro-biology gained its first great victory, and cleared forever the passage to the rational study of the natural forces which ever exert themselves in the production and in the elimination of disease.

There is a tendency to look upon the infectious maladies as the only ones in which purely biologic agencies constitute the causal factors. To be sure, they furnish our most telling illustrations, and offer many inducements for consideration. However, I wish to call attention to a more neglected and perhaps, obscure topic in illustrating the natural in disease, namely, general pathology. While the epidemic diseases are serious

indeed, with their present subjugation they do not furnish the most of our physical troubles. Yet the statement which has become almost axiomatic, that "all of the common ailments are due to the violation of physical law", is believed in only a half hearted manner. There was much wisdom shown in the physician's reply to a patient complaining from a mixture of preventable disorders, "My dear sir, you have no business to be sick". The cellular pathology of Virchow, with its various modifications, has done an immeasureable amount of good in establishing the almost imperceptible gradation existing between health and disease.

The student of general pathology soon finds that, while many conditions of the abnormal have been differentiated from the general, by finding definite specific causes for them, much remains for interpretation. In fact, the unsolved problems in general pathology are so difficult that they seem to be intangible, so intimately do they come into relation with cosmic physics, meterology, geology, sociology, chemistry, botany, zoology, and the rest that a distinguished pathologist wrote "General pathology knows no other direction, and no other order than physiology". Illustrations of this are numerous. The highly developed biceps of the blacksmith, if submitted *per se* to the pathologist, would be called a beautiful specimen of hypertrophy, but the physiologist knowing the history, sees an illustration of high development from special use. The muscle of the hypertrophied heart brought on by over-exertion, caused by some valvular or other lesion, becomes a much more serious matter. It has been shown and the fact verified by members of this Society, how active and efficient the phagocytes are in eliminating foreign particles, like bits of carbon, from the body. Pathologists have pointed out the efficiency of these same cells in defending the body against foreign invaders. In both cases, however, they are sometimes overpowered, the infection is accomplished, the abscess is formed, the disease is established, and the life may be extinguished.

It must be admitted by us all that we are too prone to overlook the influences of environment. Are we not too willing to

pass over the action of natural forces and agencies, which either consciously or unconsciously have an indwelling influence upon the vital powers of the human or the animal body? To be sure, nature has furnished us with the benefit of certain adaptations of the abnormal, but these will not suffice to sustain the body under prolonged neglect. If there is physical or mental disability, there must be a cause. If there is vigor and intellectual superiority, there is somewhere in the cosmos an explanation. Henry Clay was called a crank because he always sent the hay and grain for his trotting horses from his own farm. When questions concerning this seemingly foolish notion he replied, "When my horses eat the hay and grain from my farm, they always win, when they do not, they always lose". This was called a whim, for neither Clay nor any one else could venture a rational explanation for the fact in the statement. Finally, however, it has been found that the forage and cereals of his locality in Kentucky contain 10 per cent and upwards more phosphoric acid than those from the localities where his horses competed. If this was an isolated case, it might still be doubted that the constituents of the soil and consequently of the forage had an influence upon the vital powers of the horse. It is a verified fact, however, that those particular localities noted for raising fine animals have a forage exceedingly rich in phosphates. Again, in the early days when at least the common people lived very largely upon the crops raised on the home farm, and before there was such an interchange of food products, it is interesting to note that the localities famous for raising fine horses were equally as conspicuous for their great men. If we read carefully geographical pathology, we find in certain districts a prevalence of certain physical disabilities which as yet, fall naturally into the general group, but which nevertheless have their origin in the influence of certain local conditions.

From a study of the more general conditions which influence the animal body, one is sometimes led to feel that there is a tendency to expect too much of the microscope and to neglect naked eye observations. The old time naturalist knew little of

minute anatomy, yet we could better spare much of the microscopic than the results of the close observations of Linneus, Hunter or Agassiz. The laboratory worker loses much that the field observer takes into account. So in general pathology he who studies the abnormal in itself, fails to discover its relation to natural forces and consequently the legitimate right for its existence. Hunter and Paget showed for the first that disease begins with slight deviations from the normal, and the real cause for these deviations may be as far from the generally accepted ones as was phosphoric acid from the mind of the jockey who rode Clay's horses.

It sometimes seems unfortunate that more of our biologists do not grapple with the problems in general pathology, and circumscribe with more definite observations and experiments, the conditions which lead to the abnormal. The agencies by way of instruments and reagents are more numerous and efficient than ever before. The knowledge of physiology and physiologic chemistry is constantly increasing and the topics which need more light seem inviting. As they pertain to the living tissues, they must be approached by those who feel an inspiration for the living. The solution of the problems concerning the theories of cell-proliferation set forth by Virchow and by Weigert would be ample to fill a life time of untiring research and experiment.

No doubt, one of the great difficulties is the inability to secure sufficient material. The naturalist preserves with equal care hundreds of duplicates of the specimen which he is to study. Is this so with the physicians who are the reapers for the pathologists, and in this connection for the biologists? Are they as careful as they might be in securing the important, not necessarily the rare, specimens which from time to time fall in their way? While it is true, that the study of pathology is best carried on in connection with a large hospital service, it is equally true that much highly important and valuable material never comes to the general ward. Who has followed the voluminous literature on the cause of malignant tumors without feeling that it is quite as important to continue their study as it has been in

the past? If we are to learn more concerning the cause and nature of these abnormalities, we must continue their study. Every examination carefully made brings out new facts, or prepares better than before the examiner for the next specimen. We are told that "To him who hath, shall be given", and certainly in the material world, this applies to none better than to the devotee of the science or of the art of medicine. A distinguished oculist had successfully removed a very bad cataract and was receiving the congratulations of a brother oculist who was deeply impressed with the skill and success of the operation. "Yes", was the reply, "but that operation has cost a bushel of eyes". This tells the story of success in explaining the cause of disease quite as much as in the art of healing.

The standing difficulty in pathology has been in the relations existing between morbid anatomy and etiology. The researches of Virchow, Conheim, Stricker, and others, have shown that wherever in the body there exists an abnormal aggregation of tissue it came from pre-existing cells. Upon the cause of their proliferation, there are different theories, but concerning the fundamental biologic principles involved, all are agreed. The infectious diseases were carefully described, their periods of incubation, symptoms and gross morbid anatomy were known to the older pathologists, but they failed to distinguish the cause. The reason may be found in the trend of the biologic thought and philosophy of the day, which precluded the need of natural, or specific agencies. For this reason, the natural forces which existed as the causal factors in the epidemics or plagues of the times could not be found.

With the development of the science of bacteriology, there came a new epoch in the human understanding of the nature of diseases, especially of the infectious ones. We are prone to look upon this new science as being exceedingly modern. In its present accepted meaning this may be true, but he who finds his way through the vast literature on the subject learns that its first paper was entitled, "The world of the infinitely little", written at Delft, Holland, by Anthony Von Leeuwenhoeck in 1675. It was this man's work which was done largely for

amusement, that laid the foundation of bacteriology, a science which is now recognized as having much to do with the organic world from the lowliest of plants to the highest of the animal kingdom. For two hundred years this science was kept alive by a few workers in succeeding generations. So mysterious did it seem, that naturalists could not comprehend the effect of the labors of these infinitely little structures. But finally methods and instruments were in hand with which it was possible to isolate and study the properties of individual species among them. As soon as this came, we read in rapid succession of the discovery of the specific causes, the species of bacteria which produce relapsing fever, traumatic infections, anthrax, tuberculosis, Asiatic cholera, typhoid fever, glanders, diphtheria, and many other pests of the animal kingdom. In addition to affording us this specific information, bacteriology has had a broadening influence on the general study of disease. It has taught a perpetual co-existence and vital interdependence of plants and animals, and in some instances established a unity in the etiology of the afflictions of man and of beasts. It has also taught us that these microscopic organisms which are largely our friends, but in part our enemies, stand in a similar relationship to the flowering plants. While they in the main, prepare the food for higher vegetation, a few species among them cause the most serious of plant diseases. Thus the pear blight, a destructive disease of melons, tomatoes, potatoes, cabbage, beets, sweet corn, and of the beautiful carnation are known to be caused by certain species of bacteria.

Indirectly, bacteriology has illuminated the significance of certain phases of zoology. The student of pathology, failing to find the specific cause of certain of the infectious diseases by means of the methods of the bacteriologist, modified them somewhat, and as a result, certain higher orders of plant life and a few protozoa became distinguished as the *agens morbi* in such affections as thrush, actinomycosis, malaria, Texas or Southern cattle fever, entero-hepatitis in turkeys and a serious form of dysentery in man.

These bacteria and protozoa which sometimes become para-

sitic on the animal body are being studied, as have been studied the birds of the air, the fishes of the deep, or the beasts of the earth. These organisms of the unseen world, unknown save through the adventitious agency of the microscope, give us one of the key notes of our temporal welfare: explain to us how it is that we are able to enjoy our existence, and proclaim to us that they, these same organisms, give us permission to live. Were it not for the saprophytic bacteria, "the world would be piled mountain high with the corpses of the past dead". Their usefulness permits our living. They serve to carry back to primeval elements all our composite organisms and organizations. The deduction of Pasteur in this connection are worthy of repetition, "That wherever and whenever there is decomposition of organic matter, whether it be the case of an herb, or of an oak, of a worm or of a whale, the work is exclusively done by infinitely small organisms. They are the important, almost the only agents of universal hygiene; they clear away more quickly than the dogs of Constantinople, or the wild beasts of the desert, the remains of all that has had life; they protect the living from the dead; they do more, if there are still living beings; if, since the hundreds of centuries the world has been inhabited, life continues, it is to them we owe it".

With the knowledge brought to us by bacteriology, the progress in the study of the specific causes of disease has been rapid. Further than this, the study of the influences of these causes upon the body generally has tended to explain much that remained mysterious in general pathology. In a very few years, etiology has united all of the biologic and physical sciences and brought them within the range of the student of medicine. Etiology has become permanently linked to microbiology. We look now to botany and to zoology for the exciting causes of the infectious diseases. If we still have difficulty in understanding the nature of these maladies, let us view them in the light of parasitism. The sufferer from malaria, tuberculosis or anthrax is actually a host entertaining, at the expense of his own vital forces, a multitude of ungrateful guests in the form of microscopic plants or animals.

If we look up and down the scale of the animal and vegetable kingdoms we recognize over and over again the destructive tendencies of the living upon the living. Sometimes the scene becomes tragical as witnessed in the jungles or in the trackless deep. Sometimes the struggle is long continued and we watch for the outcome, feeling sure that without the intervention of forces guided by the intellect, the combatant which best adapts itself to the environment will eventually win. Sometimes we see the little parasitic vine slowly entwine itself about a powerful tree, drawing its substance from it until finally the life of the tree goes out. In the reservoirs of India, Koch found the water swarming with little organisms which, when taken into the human body, multiplied and gave rise to a series of symtoms and tissue changes which prostrated their host and which condition has long been known as Asiatic cholera. All of the infectious diseases, whether caused by bacteria, higher fungi or protozoa, afford illustrations of the simplest organisms becoming parasitic upon the more highly organized plants or animals. Thus it has come about that the abnormal which is seen so often in nature sometimes restricted to single individuals, sometimes appearing as devastating plagues, has been demonstrated to be the result of natural forces acting under changed conditions. The prophesies by way of the theories of Hippocrates, Sydenham and Hunter, have been fulfilled in the results of investigations carried out since the organization of this society.

If the discovery of the cause foretold the end, we could feel that, so far as the infectious diseases are concerned, the goal is near at hand. But such is not the case. Pathologists are being led step by step into broader and infinitely more complicated fields. Preventive medicine, which is the key note of modern medicine, is clamoring for more definite, specific knowledge concerning the possibilities of not only recognized pathogenic bacteria, but of others as well. Health officers are asking for information concerning the possible means of infection, and epidemics and epizootics of peculiar character are constantly appearing and demand interpretation. Then come

the numerous questions concerning the relationship and identity of certain animal and human diseases. Comparative and experimental pathology, which have become a necessity in the interpretation of certain human affections, have laid at our door a series of problems, so long and so difficult, that the most hopeful read the subjects of research for generations to come. Every practical investigation in comparative pathology brings to light a host of problems, perhaps of secondary importance, but clamoring for attention.

I have already referred to the significance of etiology. I desire to call attention to a few important illustrative results in comparative etiology. In an old pathology we learn that formerly tuberculosis, glanders and actinomycosis, all diseases of the lower animals and all affections of man, are very closely related if not identical. They were grouped together. Now we know that the bacteria of glanders and tuberculosis and the fungus of actinomycosis, are as different as three species of the flowering plants. Recently, five diseases of swine known to the veterinarians of Europe, were positively demonstrated by Jensen to be caused by the bacillus of rouget, and thus varieties of one and the same disease. With the existence of definite etiological factors, the isolating and grouping of diseases must continue until they are classified in accordance with this standard. Some one asks what difference does it make? The answer must be first, that right is right; and secondly, when all of these diseases are treated directly or indirectly with some product of their specific organisms as in the case of diphtheria antitoxin of today, we cannot hope for good results save in cases of disease, no matter about its form, which are due to the same etiological factor.

This lead us to the cause for the variation in the course of infectious diseases. The difficulty of becoming enlightened on this highly important topic, without resource to experimental pathology is obvious. By its aid much has been learned concerning the fundamental principles involved, although this field has just been opened. The causes may be cast in a simple equation, namely, the course of the disease will change in ac-

cordance with variation in either the resistance of the animal or the virulence of the specific bacteria. Thus, for example, the bacterium of an acute septicaemia which should ordinarily cause death in a rabbit in eighteen hours, may be changed so that the lesions may become peritonitis, pleuritis, pericarditis, subcutaneous or deeper seated abscesses. In swine we often see abscesses in joints due to the localization of bacteria which ordinarily cause an acute general disease, but which owing either to their attenuation or to the resistance of the host, have produced painful and long suffering localized affections. In human pathology, such localized lesions are common and the desirability of extending similar investigations with the etiological factor of all of the infectious diseases is apparent. The formula is simple; but define for us who can, the range of influences which may modify that subtle property of bacteria we call virulence. What elements in the body impart to it a natural resistance? Really, what are these vital forces about which men talk so freely and know so little?

If we pass below these more superficial but perplexing questions, we are met with those concerning the influence of the host upon the parasite. One of them has already found expression in the assertion that "the continued passage of a species of bacteria through a single species of animals, tends to increase its virulence for that species and to attenuate it for all others". This hypothesis, which needs to be verified, is one of vital importance respecting the transmission of infectious diseases, such for example as tuberculosis from animals to man and *vice versa*. If we could continue to call up questions in this department, which are still unanswered, we would soon learn that notwithstanding the much already known, all of the articles in the final constitution of preventive or sanitary medicine have not been written. Schools and theories of medicine which were largely based on individual opinions are rapidly disappearing and the science of medicine, which governs its practice, is being constructed in accordance with the results of the biologic study of disease.

The unanswered questions are not all concerning etiology. Before the ideals of the most far seeing advocates of preventive medicine are realized, millions of individuals will have become infected and their restoration to health is the final demand upon the physician. The trend of therapeutics in the line of serum therapy is well known. The marvelous success with diphtheria antitoxin gives hope that somewhat similar methods will bring about like results with other maladies. The problems here are numerous and nowhere in the realm of human research is there a field involving such a variety of factors. Physiology, chemistry, physics, all have their share to do in this field ot applied biology. "Surely there is as much pure gold of science to be gathered in working out these problems applicable to the every day life of the individual and to the State as in other kinds of inquiry aimed at a supposed higher mark".

I have tried in this short address to bring to your attention certain very general considerations concerning the inseparable relations existing between disease and the acting forces of nature. It has been possible to touch upon only a few of the many topics which suggested themselves, and these inadequately. We have seen, however, that many diseases depend for their existence upon well defined biologic agencies, while others seem to take origin in the influence of a greater variety of forces. It is to the interpretation of these as yet obscure factors in the production and in the healing of disease that future research will, in part at least, be directed. Although many of these investigations seem to be independent of the microscope and microscopic methods, others and equally important ones rely entirely for their success upon them. More than this, the every-day application of the existing knowledge of the nature and cause of disease require the constant use of the microscope and the fullest interpretation of the facts call for still better methods. As we return to our accustomed places let us take up with renewed zeal the struggle with the problems in hand, not wavering for the reason that Browning gives:

"Knowing ourselves, our world,
Our task so great,
Our time so brief".